FIG. 1A

16		AGGG	ACGGTCGTGA	GACAC TICCAIGGIG ACGGICGIGA AGGG	ATGGTGACAC	ACAGGCTGCA ATGGT
12	ATTTTCATTT	TGACTTGCAT	TTTATTTGT	TICATITITC	GACAGICITI ICTIAGCAIC IICATITITC ITTAITITGI IGACTIGCAI AITITCAITI	CAGICITI
~	TCTTTCAACA	TTTGATAGAT	TGTGTTTTCT	ATGTTCCAAT	GTGTCTGGGC GGAGCAAAT ATGTTCCAAT TGTGTTTCT TTTGATAGAT TCTTTCAACA	GTCTGGGC

FIG. 1B

TGATGATGAA	AAGAAAGTGA	TGATGATGAA AAGAAAGTGA CAGGTGGTCG AAATGGCTAT GGAGCCAAAT TGTGTAACAT	AAATGGCTAT	GGAGCCAAAT	TGTGTAACAT	120
ATTCAGTACC	AAATTTACTG	ATTCAGTACC AAATTTACTG TGGAAACAGC CAGTAGAGAA TACAAGAAAA TGTTCAAACA	CAGTAGAGAA	TACAAGAAAA	TGTTCAAACA	180
GACATGGATG	GATAATATGG	GACATGGATG GATAATATGG GAAGAGCTGG TGA	TGA			213

FIG. 1C

18		•				E
18	TTCCTATTAT	GAATGGTACA	TGTTGAGCCT	ACAACCAGCG	GTTGAAGTTT TTATATGATG ACAACCAGCG TGTTGAGCCT GAATGGTACA TTCCTATTAT	GTTGAAGTTT
12	ATGATCACAC	CCACCAAAAG	ATTGTTATTT	CTTTGGCTCG	CATCTITACA AIGCICAGCI CITIGGCICG AITGITAITI CCACCAAAAG AIGAICACAC	CATCTTTACA
9	GTCCACGATA	GATTCTGCTA	TGGTGGCAAG	CCAGGCTACA	GCCCATIGGT CAGITIGGTA CCAGGCTACA IGGIGGCAAG GAITCIGCTA GICCACGATA	GCCCATTGGT

FIG. 1D

224		GAAG	GATTAGTGGT	CCAA ATCAATATGT GATTAGTGGT GAAG	CTGGCTCCAA	TATTGAAGAA CTGGCT
180	TCAAGGGTAC	GAAC CITIGCCAAI GCIICCAAGI IACAAGAACI ICAAGGGIAC	GCTTCCAAGT	CITIGCCAAL	GGAGAAGAAC	TTTGATGGAT GGAGAA
120	ACATCAGGCG	ATCC CCAACTTTGA TGTGCGTGAA ATTGTAAATA ACATCAGGCG	TGTGCGTGAA	CCAACTTTGA	TGCAAA	TGGGTGGTCC
09	GAATCGGTAC	ATTCCTATTA TTCCCATGGT GCTGATAAAT GGTGCTGAAG GAATCGGTAC	GCTGATAAAT	TTCCCATGGT	ATTCCTATTA	TGAATGGTAC

FIG. 1E

32				AAACTGGCA	PTGTGAAGAT GACTGAAGAA AAACTGGCA	TGTGAAGAT
30	GTGAAATTTG	AGATACCACT	AATACCATAC	GACTATAGGG	AGACACCICC TCTCATAACA GACTATAGGG AATACCATAC AGATACCACT GTGAAATTTG	AGACACCICC
24	GGCACCGAGA	CATGTTGAAT	TTCTAGAACC	AAAGAACAAG	SAACATGGAC CCAGACATAC AAAGAACAAG TTCTAGAACC CATGTTGAAT GGCACCGAGA	SAACATGGAC
18	CTTCCCGTCA	AATCTCAGAG	CAACCATTGA	CTTAATTCTA	TAGTGGTGA AGTAGCTATT CTTAATTCTA CAACCATTGA AATCTCAGAG CTTCCCGTCA	TAGTGGTGA
12	CAATATGTGA	GGCTCCAAAT	TTGAAGAACT	AAGGGTACTA	TICCAAGITA CAAGAACITC AAGGGTACTA ITGAAGAACI GGCTCCAAAI CAATAIGIGA	TCCAAGTTA
9	TTGCCAATGC	AGAAGAACCT	TGATGGATGG	ATCAGGCGTT	rgcgtgaaat tgtaaataac atcaggcgtt tgatggatgg agaagaacct ttgccaatgc	GCGTGAAAT

FIG. 1F

19					AGCC	AGATAAAGCG
18	ATTTTCTCTA	TTTGCCATCT	CAATGATTAT	GGCTTATTT	CTTTAATTAA TTCTTTCTTA GGCTTATTTT CAATGATTAT TTTGCCATCT ATTTTCTCTA	CTTTAATTAA
12	TGAATCAGAA	ATATCCCCTC	GATCCGAATC	GCCTTCACAG	TICITICCAG GCCTICACAG GAICCGAAIC ATAICCCCIC IGAAICAGAA	TTTGCTGGGC
0	TCTGGAACCT	TTCTTCTTCA	TCTCTTCATT	TCGTTGTCAC	AGTTTCCTTT TCGTTGTCAC TCTCTTCATT TTCTTCTTCA TCTGGAACCT	CACTCTTTTC

FIG. 1G

20				ATCTGA	GCCAAGTCTT CTTTCCACAA ATCTGA	GCCAAGTCTT
18	AATAAATGTA	CCAATTCTTC	TCAACAGCCT	CCGACTTGTT CATCTTGTTT TTCCTTGGCT TCAACAGCCT CCAATTCTTC AATAAATGTA	CATCTTGTTT	CCGACTTGTT
12	CCCAGGAAGT	TCCCCCCTTT	CCCTTGGCCT	GGCAAAACTT CAGCCATTTG TGTTTTTTC CCCTTGGCCT TCCCCCCTTT CCCAGGAAGT	CAGCCATTIG	GGCAAAACTT
9	ACGCGGAGAA	CTCTTTGACC	CGTGGAATGA	TCTGCCTCTG CTTTCATTTC TATGGTTATT CGTGGAATGA CTCTTTGACC ACGCGGAGAA	CTTTCATTTC	TCTGCCTCTG

FIG. 1H

19					CTCG	SGCTCTGTTT CTCG
18	TGCTCTCCGT	TTTTTGTTGC	GTGAATTTTG	GAATC CAAATCCATT GTGAATTTTG TTTTTGTTGC TGCTCTCCGT	CATCTGAATC	SAGAAATCTT CATCT
12	ATCAAAATCT	CAGITITITC	TCTTCATCAT	TCTGA TGGGACAAA TCTTCATCAT CAGTTTTTTC ATCAAAATCT	TAGCATCTGA	TTAGGTGGAC TAGCA
9	AGTTTTGGTC	GTTTTGGGGA	TTGTTACTAA	TGTGG TTTCAGTTCT TTGTTACTAA GTTTTGGGGA AGTTTTGGTC	TTTTCTGTGG	SACACGACAC TTTTC

24						IC
24	AGCTTTGAAT	AAAGGGATCC	AAAGGAACTA	GGCTGCCCCA	ACTACCGGTG CCAAAAAAG GGCTGCCCCA AAAGGAACTA AAAGGGATCC AGCTTTGAAT	ACTACCGGTG
18	TTCCACCTCC	AAAGTCAGTC	ACAGCAGCAA	TGTGAC AGTGAAGAAG ACAGCAGCAA AAAGTCAGTC TTCCACCTCC	AGAATGTGAC	GTTCCTAAAA AGAA
7.	TACAAACCCA	AAACTGAAAT	TTCCCAGATG	TGCTACACAT	SCACTGTCTT CAAGCCCTCC TGCTACACAT TTCCCAGATG AAACTGAAAT TACAAACCCA	CCACTGTCTT
•	GGCAGTGT.A	ATGATGTTAA	CTTGAAGCTG	AAGTGT CGTGTCAGAC CTTGAAGCTG ATGATGTTAA GGGCAGTGTA	AGAAAAGTGT	CTGAAACCAC AGAA

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FIG. 1J

22(GGTCTGACAC	CATCA TCAGCTTCAA GGTCTGACAC	CTTAACATCA	GTACACTGCC CTTAA
18(GAAGACAGTG	CAGTT TCATCTGGGA AATGTGTAGC AGGAGGGCTT GAAGACAGTG	AATGTGTAGC	TCATCTGGGA	AATTTCAGTT	CTGGGTTTGT AATTT
12(TTTTAGGAA	TGTCACATTC	TCTTCTTCAC	TTTGCTGCTG	TGGAGGTGGA AGACTGACTT TTTGCTGCTG TCTTCTTCAC TGTCACATTC TTTTTAGGAA	TGGAGGTGGA
9	GCACCGGTAG	CCCIT TIAGIICCII IIGGGGCAGC CCITITITIG GCACCGGIAG	Tregeccaec	TTAGTTCCTT	TGGATCCCTT	AATTCAAAGC TGGAT

Figure 1K

60 120 180 220 CTGGGTTTGT AATTTCAGTT TCATCTGGGA AATGTGTAGC AGGAGGGCTT GAAGACAGTG GTACACTGCC CTTAACATCA TCAGCTTCAA GGTCTGACAC AATTCAAAGC TGGATCCCTT TTAGTTCCTT TTGGGGCAGC CCTTTTTTTG GCACCGGTAG TGGAGGTGGA AGACTGACTT TTTGCTGCTG TCTTCTTCAC TGTCACATTC TTTTTAGGAA

Figure 1L

GTGTTGAGCC TGAATGGTAC ATTCCTATTA TTCCCATGGT GCTGATAAAT GGTGCTGAAG GAATCGGTAC TGGGTGGTCC TGCAAATCC CCAACTTTGA TGTGCGTGAA TTGTAAATA ACATCAGGCG TTTGATGGAT GGAGAAGAAC CTTTGCCAAT GCTTCCAAGT

60 120 170

FIG. 2A

RANDOM FRAGMENTATION

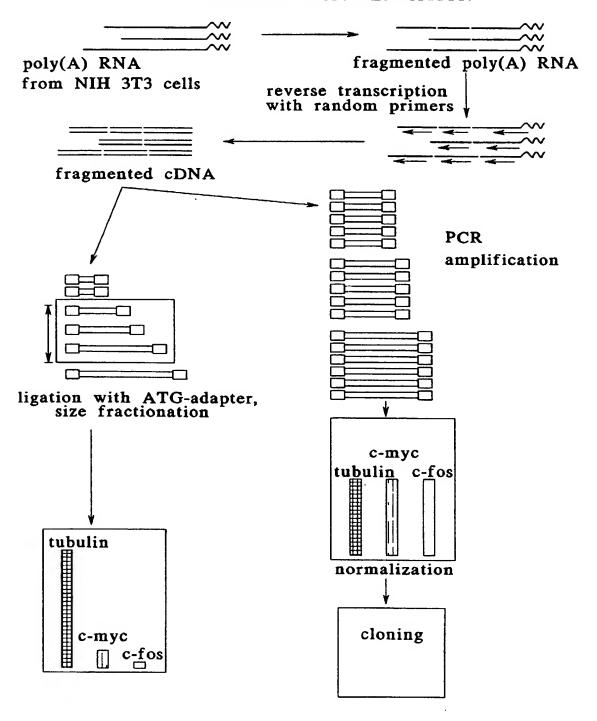


Figure 2B

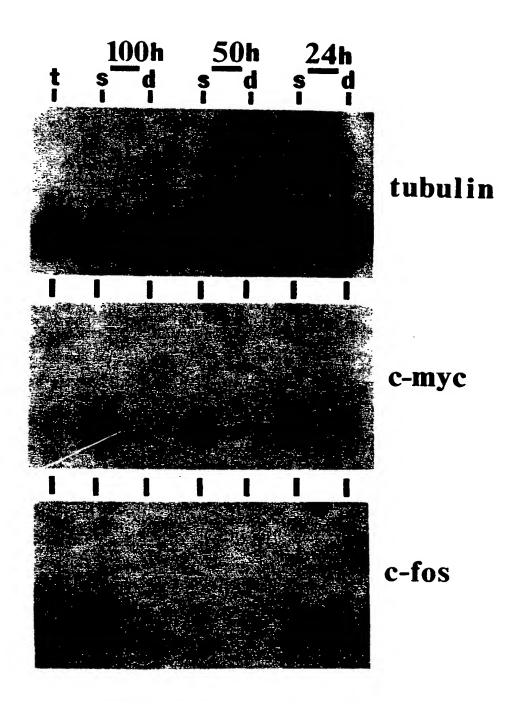


FIG. 3A

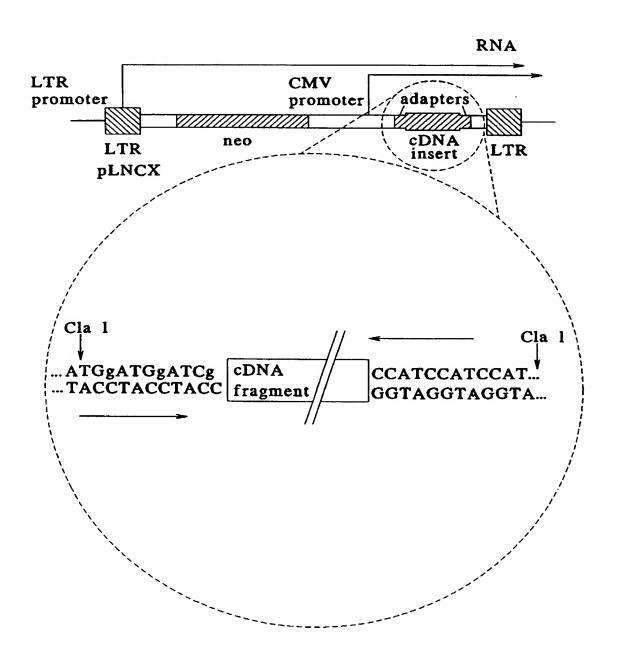
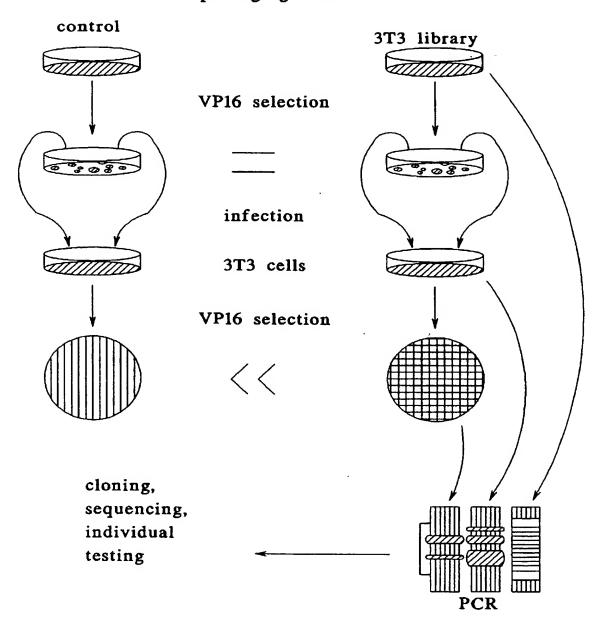
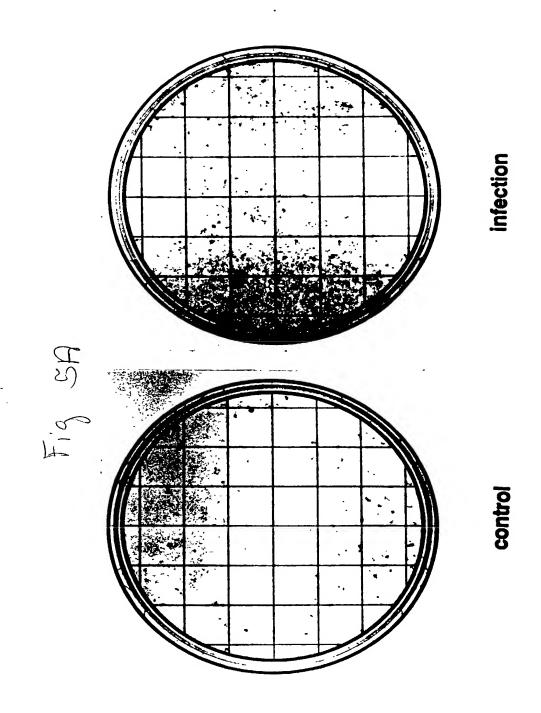


FIG. 3B



Mixture of Eco and Ampho packaging cells





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VP16 selection

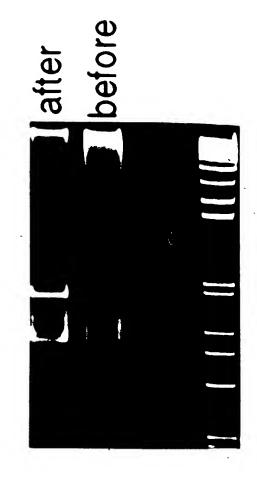


Fig. 5B

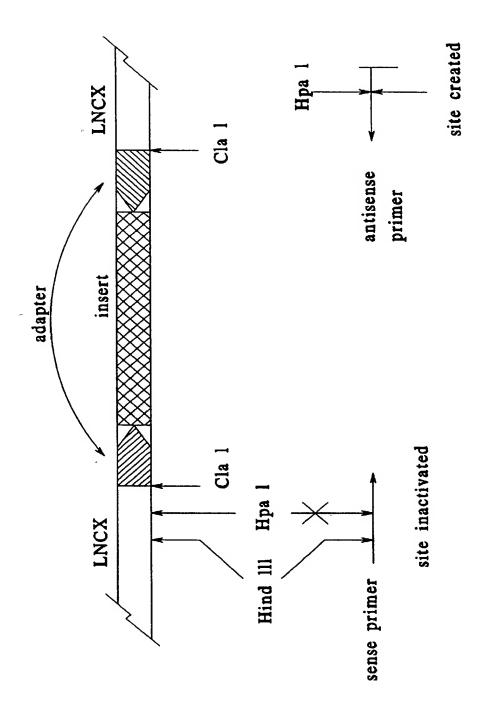
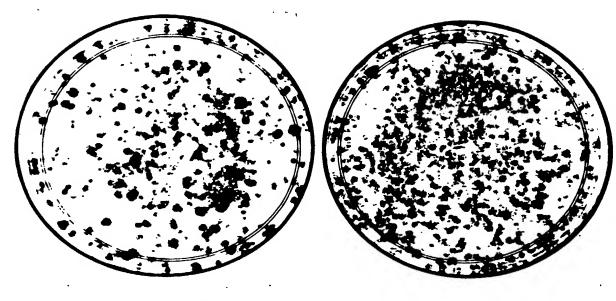


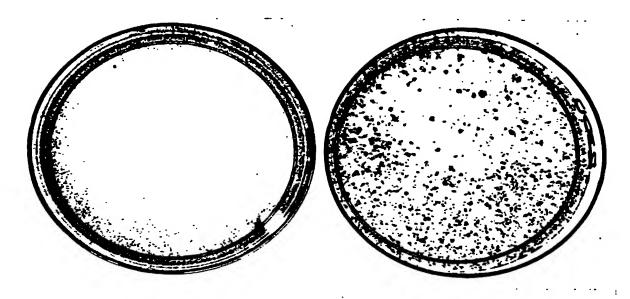
Figure 7A



insert-free vector

VPA

Figure 7B



insert-free vector

VP9-11

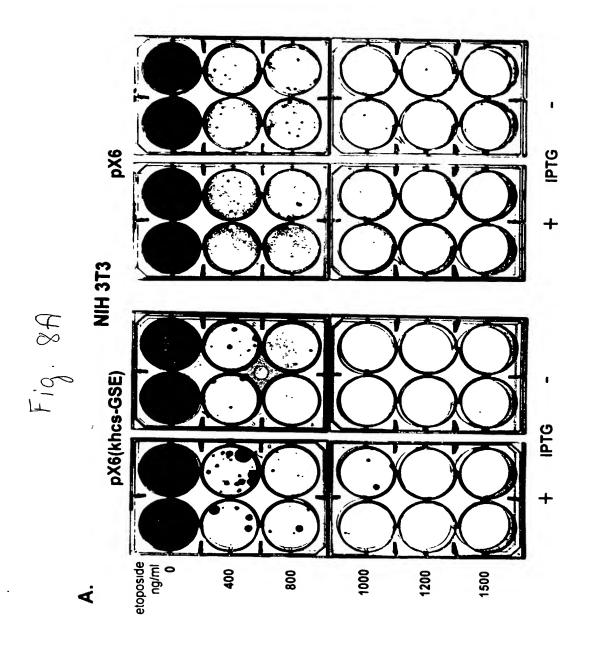
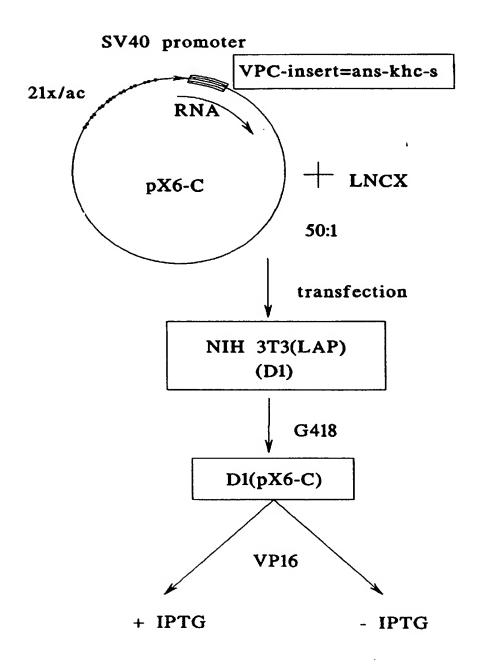


FIG. 8B



327				AGCCACT	AACGGTTTAG CTCGTTTTCC AGCCACT	AACGGTTTAG
300	CCGTTACGCC	CACTGTCTCC	CATCAATAGG	TCAAACTGCT	SCAAATTAGC TITCICITIG ICAAACIGCI CAICAAIAGG CACIGICICC CCGIIACGCC	CCAAATTAGC
240	GTGAAGGCTT	TITATCCGCT	TAGCAATATC	TCACTGGTAA	CGACTGCAGC AGCTGGTTA TCACTGGTAA TAGCAATATC TTTATCCGCT GTGAAGGCTT	CGACTGCAGC
180	CCAGCCATTC	GGTAAAACTA	TTTCAGCATC	CACTITCTIC	ATTIAGCAAG TICTICTICA CACTITCTIC TITCAGCAIC GGIAAAACIA CCAGCCAIIC	ATTTAGCAAG
120	TGTTTATACA	GTCATCAAGT	CTTCATCCTT	TGGTTAATCT	TCTCTACCAA TIGGCTTIGT IGGTTAAICT CTTCATCCTT GTCATCAAGT IGTTTATACA	rctctaccaa
)9	ATCTTCAATT	CAGCATTIGT	CTTCCTGATC	GCCAGAAGCT	CTTGATCCCT TCTGGTTGAT GCCAGAAGCT CTTCCTGATC CAGCATTTGT ATCTTCAATT	CTIGAICCCI

ccGAccGGGA	GCGGGAGAAG	CCGACCGGGA GCGGGAGAAG GAGCGGGAGC GGGAGCAGCG GGAGAAGGAG CGGGAGAAGG	GGGAGCAGCG	GGAGAAGGAG	CGGGAGAAGG)9
AGCTGGAGCG	CGACGGGAGA	AGCTGGAGCG CGACGGGAGA AGGAACGGGA GCGCGAGCTG GAGCGGCAGC GGGAGCAGCG	GCGCGAGCTG	GAGCGGCAGC	GGGAGCAGCG	12(
GGCGAGGGAG	AAGGAGCTGC	SGCGAGGGAG AAGGAGCTGC TGGCTGCCAA GGCCTTAGAG CCCACCACCT TCCTGCCTGT	GGCCTTAGAG	CCCACCACCT	rccreccrer	18(
GGCCGAGCTG	CACGGACTCC	SGCCGAGCTG CACGGACTCC GAGGTCACAG CACGGAGGAG CGGCCCAAGC CCTCGGAGCA	CACGGAGGAG	CGGCCCAAGC	CCTCGGAGCA	24(
GCTGACCCCA						250

20				AGTAGC ACGAGGCC	ATGAAGTAGC	SCTAGTACAG ATGA
18	CAGAGATGAA	AACAACTCTT	GGCCCTGCTC	AGTCCTTGGT	SCCTGACTCC ACCGAAGTCG AGTCCTTGGT GGCCCTGCTC AACAACTCTT CAGAGATGAA	CCTGACTCC
12	CCIGCTICCG	CCTGACCATC	GATTTTGAAC	AGGAGGGCAA	SATGCAGACC TGCATGTCCG AGGAGGGCAA GATTTTGAAC CCTGACCATC CCTGCTTCCG	SATGCAGACC
9	TTGAGACTTG	GICCCCTICT	AGGAGAAGGA	AGTCGAGCTC	CTCAGAGGTG ATCCTCTGGG AGTCGAGCTC AGGAGAAGGA GTCCCCTTCT TTGAGACTTG	CTCAGAGGTG

FIG. 12A

CGACAAACAT	CATCTGGGAA	CATCTGGGAA GACCCACACG ATGGAGGGTA AACTTCATGA TCCAGAAGGC	ATGGAGGGTA	AACTTCATGA	TCCAGAAGGC	09
ATGGGAATTA	TTCCAAGAAT	TICCAAGAAT AGTGCAAGAT ATTTTAATT ATATTTACTC CATGGATGAA	ATTTTTAATT	ATATTTACTC	CATGGATGAA	120
AATTTGGAAT	TTCATATTAA	TTCATATTAA GGTTTCATAT TTTGAAATAT ATTTGGATAA GATAAGGGAC	TTTGAAATAT	ATTTGGATAA	GATAAGGGAC	180
TTGTTAGATG	TTTCAAAGAC	TITCAAAGAC TAACCITICA GICCAIGAAG ACAAAAACCG IGIICCCIAI	GTCCATGAAG	ACAAAAACCG	TGTTCCCTAT	240
GTAAAGGGGT	GCACAGAACG	GCACAGAACG TITCGIGIGI AGICCAGAIG AAGICAIGGA IACCAIAGAI	AGTCCAGATG	AAGTCATGGA	TACCATAGAT	300
GAAGGGAAAT	CCAACAGAGA	CCAACAGAGA TGTCGCAGTT ACAAATATGA ATGAACATAG CTCTAGGAGC	ACAAATATGA	ATGAACATAG	CTCTAGGAGC	360
CACAGCATAT	TTCTTATTAA	TTCTTATTAA TGTAAAACAA GAGAATACAC AAACGGAACA GAAACTCAGT	GAGAATACAC	AAACGGAACA	GAAACTCAGT	420
GGAAAGCTTT	ATCTGGTTGA	ATCTGGTTGA TTTAGCTGGC AGTGAGAAGG TTAGTAAGAC TGGGGCTGAA	AGTGAGAAGG	TTAGTAAGAC	TGGGGCTGAA	480
GGTGCTGTGC	TGGATGAAGC	TGGATGAAGC TAAGAACATC AAGAAGTCAC TTTCTGCACT TGGAAATGTC	AAGAAGTCAC	TTTCTGCACT	TGGAAATGTC	540
ATTTCTGCTT	TGGCAGAGGG	TGGCAGAGGG CAGTACCTAT GTTCCTTATC GAGATAGTAA AATGACCAGA	GTTCCTTATC	GAGATAGTAA	AATGACCAGA	009
ATTCTTCAAG	ATTCATTAGG	ATTCATTAGG TGGCAACTGT AGGACCACTA TTGTCATATG CTGCTCTCCA	AGGACCACTA	TTGTCATATG	CTGCTCTCCA	099
TCATCATACA	ATGAGTCTGA	ATGAGTCTGA GACAAAGTCA ACACTCCTCT	ACACTCCTCT	TTGGTCAAAG GGCCAAAACA	GGCCAAAACA	720
ATTAAGAACA	CAGTCTGTGT	CAGTCTGTGT CAATGTAGAG TTAACTGCAG AGCAGTGGAA AAAGAAGTAT	TTAACTGCAG	AGCAGTGGAA	AAAGAAGTAT	780

FIG. 12B

GAAAAAGAAA	GAAAAAGAAA AGGAAAAAA TAAGACTCTA CGGAACACTA TTCAGTGGCT GGAAAACGAG	TAAGACTCTA	CGGAACACTA	TTCAGTGGCT	GGAAAACGAG	84
CTAAACCGTT	CTAAACCGTT GGCGTAACGG GGAGACAGTG CCTATTGATG AGCAGTTTGA CAAAGAGAAA	GGAGACAGTG	CCTATTGATG	AGCAGTTTGA	CAAAGAGAAA	90
GCTAATTTGG	GCTAATTTGG AAGCCTTCAC AGCGGATAAA GATACTGCTA TTACCAGTGA TAAACCAGCT	AGCGGATAAA	GATACTGCTA	TTACCAGTGA	TAAACCAGCT	96
GCTGCAGTCG	GCTGCAGTCG GAATGGCTGG TAGTTTTACC GATGCTGAAA GAAGAAAGTG TGAAGAAGAA	TAGTTTTACC	GATGCTGAAA	GAAGAAAGTG	TGAAGAAGAA	102
CTTGCTAAAT	CTTGCTAAAT TGTATAACA GCTTGATGAC AAGGATGAAG AGATTAACCA ACAAAGCCAA	GCTTGATGAC	AAGGATGAAG	AGATTAACCA	ACAAAGCCAA	108
TTGGTAGAGA	TTGGTAGAGA AATTGAAGAC ACAAATGCTG GATCAGGAAG AGCTTCTGGC ATCAACCAGA	ACAAATGCTG	GATCAGGAAG	AGCTTCTGGC	ATCAACCAGA	114
AGGGATCAAG	AGGGATCAAG ATAATATGCA AGCTGAACTG AATCGCCTCC AAGCAGAAAA TGATGCTTCT	AGCTGAACTG	AATCGCCTCC	AAGCAGAAAA	TGATGCTTCT	120
AAAGAAGAAG	AAAGAAGAAG TCAAAGAAGT TTTACAGGCC TTAGAGGAAC TGGCTGTTAA TTATGATCAG	TTTACAGGCC	TTAGAGGAAC	TGGCTGTTAA	TTATGATCAG	126
AAGTCTCAGG	AAGTCTCAGG AAGTTGAAGA CAAAACAAAG GAATATGAAT TGCTTAGTGA TGAATTGAAT	CAAAACAAAG	GAATATGAAT	TGCTTAGTGA	TGAATTGAAT	132
CAAAAATCTG	CAAAAATCTG CAACTTTAGC AAGTATTGAT GCTGAGCTTC AGAAGCTGAA GGAAATGACC	AAGTATTGAT	GCTGAGCTTC	AGAAGCTGAA	GGAAATGACC	138
AACCACCAGA	AACCACCAGA AGAAACGAGC AGCTGAAATG ATGGCATCAT TATTAAAAGA CCTTGCAGAA	AGCTGAAATG	ATGGCATCAT	TATTAAAAGA	CCTTGCAGAA	144
ATAGGAATTG	ATAGGAATTG CTGTGGGGAA TAACGATGTG AAGCAACCAG AAGGAACTGG TATGATAGAT	TAACGATGTG	AAGCAACCAG	AAGGAACTGG	TATGATAGAT	150
GAAGAGTTTA	GAAGAGITTA CIGITGCAAG ACTCTACATT AGCAAAATGA AATCAGAAGT AAAGACCATG	ACTCTACATT	AGCAAAATGA	AATCAGAAGT	AAAGACCATG	156

FIG. 12C

238		GTCAGCCCG	AAGCTTTGGA	GAAAGAGTGA	AACGGCTTAG AGCTACTGCA GAAAGAGTGA AAGCTTTGGA GTCAGCCCG	AACGGCTTAG
234	AAGTTAGAGA	TGAGCTTCCT	ATCTTCGCTG	GATAATGCAG	TGCACAAGCA GTTGGTACGT GATAATGCAG ATCTTCGCTG TGAGCTTCCT AAGTTAGAGA	TGCACAAGCA
228	CTCACCAAAG	CCTTGAACAG	TTGAAAACAA	ATCTCCTTCC	GIGCIGCACA GAAGCAGAAA AICTCCTICC TIGAAAACAA CCTIGAACAG CTCACCAAAG	GTGCTGCACA
220	ACTGGCGGCA	CTCTGACGAC	CCGAGGTCGA	CTACCAGGGT GAAAAAGAGG CCGAGGTCGA CTCTGACGAC ACTGGCGGCA		CAGGACTTGG
216	GCTCTTTGTT	ACCTGCGTAA	ACTITACACA	AGAACTTCAG	TIGGAGGAGA CCGIGGCAAA AGAACTICAG ACTTIACACA ACCIGCGIAA GCICTIIGII	TTGGAGGAGA
210	CTTGAAGGGT	CAAGACAAGA	CGAGAACAAG	GCAAGACAGA	CTGCATGAGC TCACGGTTAT GCAAGACAGA CGAGAACAAG CAAGACAAGA	CTGCATGAGC
204	GAGCAGGAAG	ACCAAGAGAA	AAGGCTACAG	TGAGAGGCTG	GAACGGCTAA GGGTGGAGCA TGAGAGGCTG AAGGCTACAG ACCAAGAGAA GAGCAGGAAG	GAACGGCTAA
198	GTTGGAGCAG	AGAAGATGGT	GACCAAAACC	TGACCTCCAA	GCAAAGGAAA AGCTAATCAC TGACCTCCAA GACCAAAACC AGAAGATGGT GTTGGAGCAG	GCAAAGGAAA
192	TGAAGTTGAG	GCTTGCGAGA	CAAATCAGTA	CCACCAAAAA	ATCCAGAGTC ACAGAGAAAC CCACCAAAAA CAAATCAGTA GCTTGCGAGA TGAAGTTGAG	ATCCAGAGTC
186	TGAGCAGCAG	AGCAAGCTGT	AATGAAGTCA	TCAGACTGCA	AAAGAGCACT TGAACAAGGT TCAGACTGCA AATGAAGTCA AGCAAGCTGT TGAGCAGCAG	AAAGAGCACT
180	TGAAATGGAA	AGAAAGTCCA	CGAGCACAAG	GIGAGGAGCI AGICCAACIC CGAGCACAAG AGAAAGICCA IGAAAIGGAA	GTGAGGAGCT	GATTCCCTTG
174	GGAATCTGTT	GGCAGCTGGA	CAAAAGAAGA	AGTACCTTCA GAATGTAGAA CAAAAGAAGA GGCAGCTGGA GGAATCTGTT	AGTACCTTCA	TCACTGACTG
168	CAAAATCAAG	CGGATCTCCC AACATGAAGC CAAAATCAAG		ATGCCAGCTT	AATGAGAAAG AGTTAGCAGC ATGCCAGCTT	AATGAGAAAG
162	AATGGAAGAA	GCAACAAAAA	CAGACTGAGA	AGAAAGCACG	GTGAAACGCT GCAAACAGCT AGAAAGCACG CAGACTGAGA GCAACAAAAA AATGGAAGAA	GTGAAACGCT

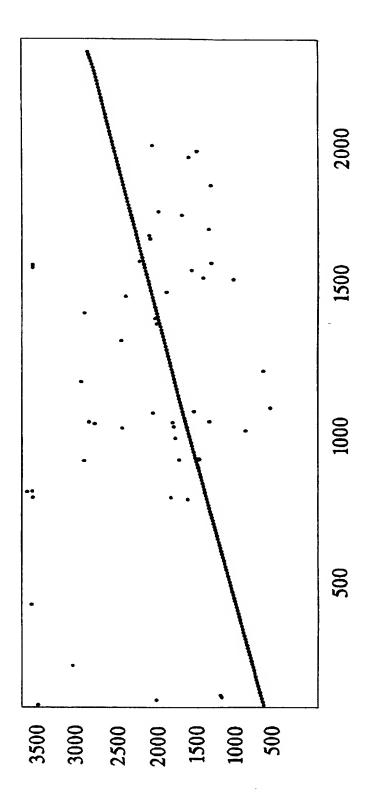


FIG. 13B

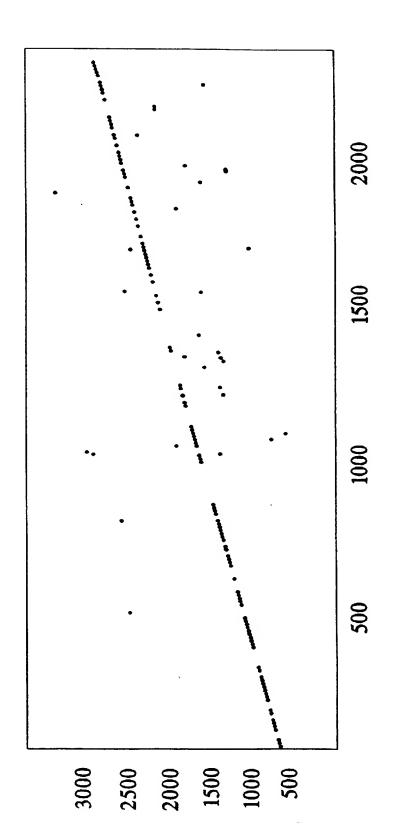


FIG. 13C

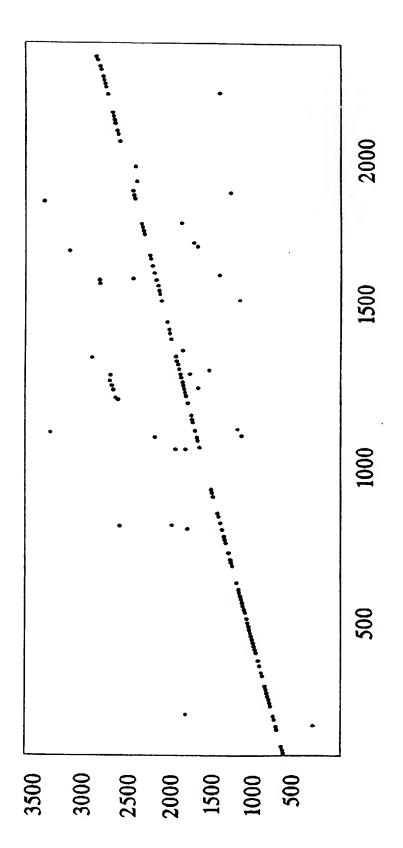


FIG. 13D

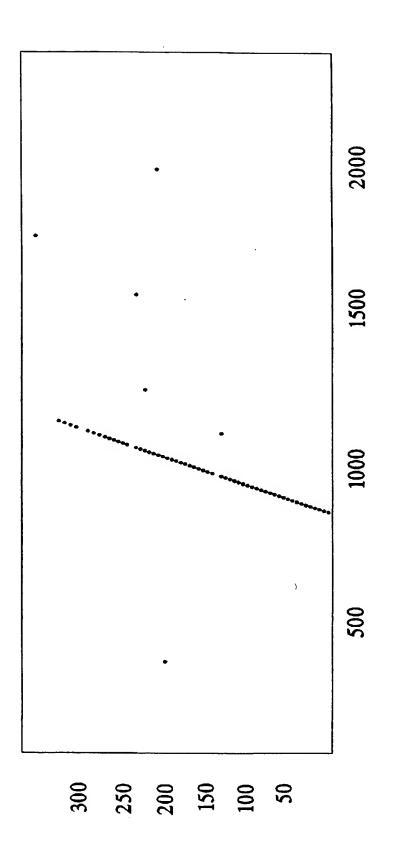
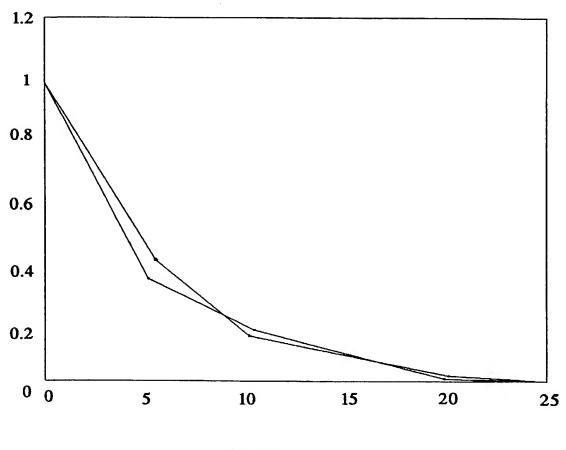


FIG. 14A



Act D [μg/mL]

FIG. 14E

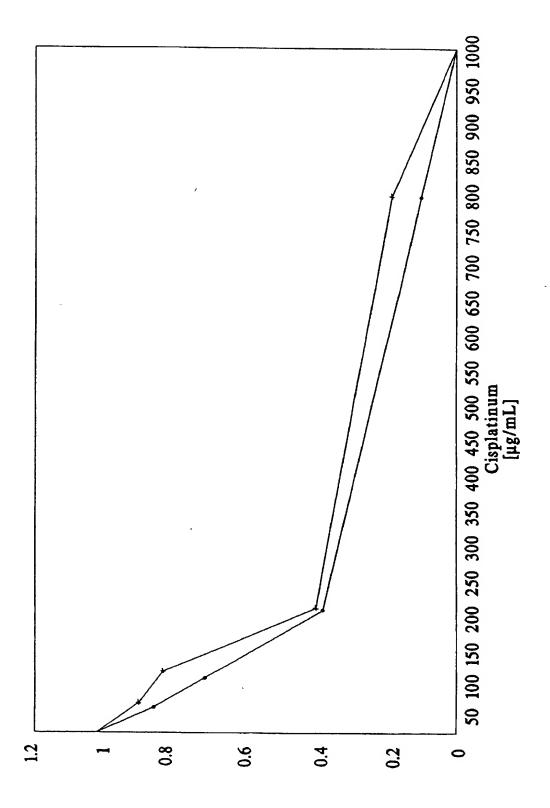


FIG. 14C

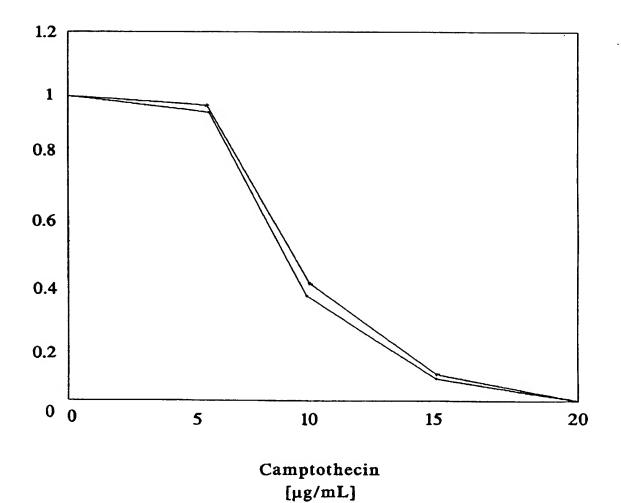


FIG. 14D

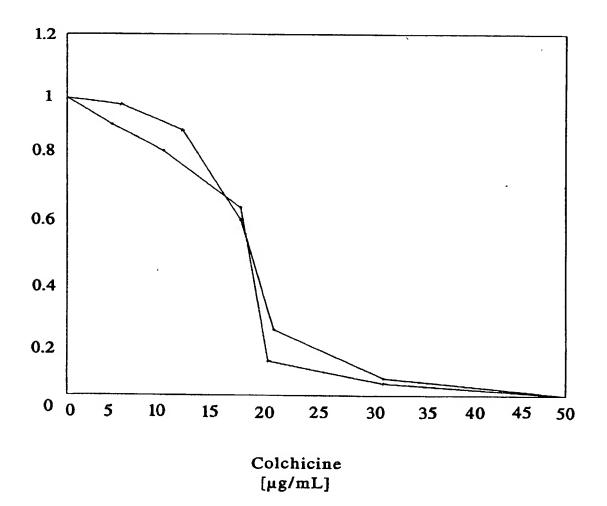
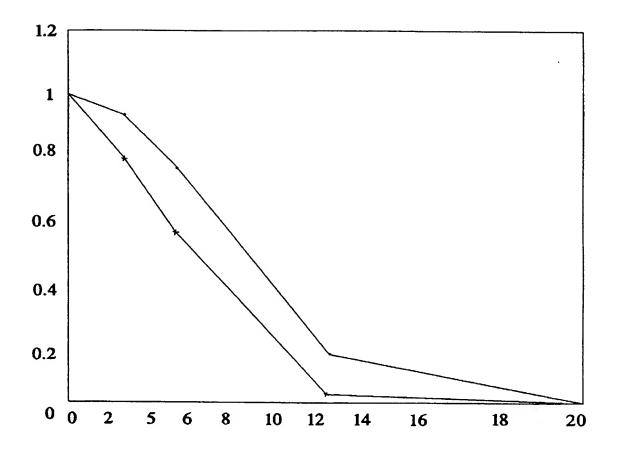
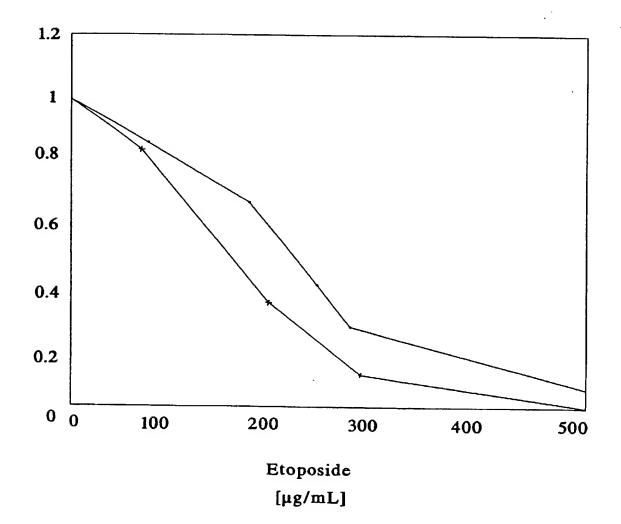


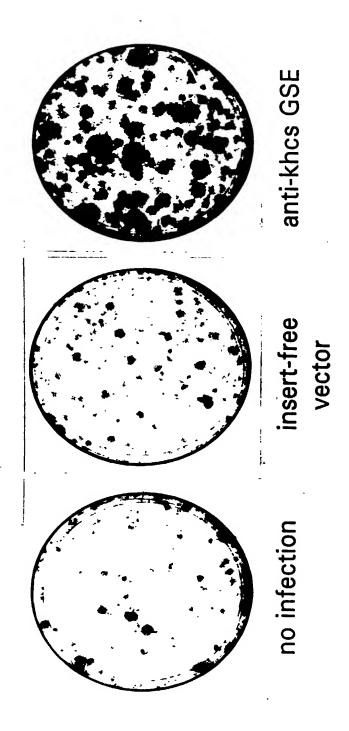
FIG. 14E



Adriamycin [µg/mL]

FIG. 14F





F1815

Figure 16

